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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/983,067	10/23/2001	Akio Inoue	1752-0151P	8894

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EXAMINER	
MAYER, SUZANNE MARIE	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 11/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/983,067	INOUE ET AL.	
	Examiner	Art Unit	
	Suzanne M. Mayer, Ph.D.	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17,19 and 20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☒ Claim(s) *19 and 20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10-04-2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Applicants have cancelled claim 18 and added claims 19-20. Claims 1-17 and 19-20 are pending.

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted on October 4, 2005 has been considered by the examiner. See signed and attached PTO-1449.

Withdrawal of Objections/Rejections

3. Any rejection and/or rejection cited in the previous Office action and not restated below is withdrawn.

Maintained Rejections/Objections

Claim Rejections - 35 USC § 102

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Claims 1-17 are rejected under 35 U.S.C. 102(e) as being anticipated by Rothschild et al. (US 6,306,628 and 2005/0032078). The details of the rejection are outlined in the previous Office action.

Response to Arguments

35 USC § 102(e)

6. Applicant's arguments filed August 18, 2005 have been fully considered but they are not persuasive.

Applicant assert that Rothschild et al. do not teach the claimed embodiments of the invention. Specifically, it is argued that because at least one (or as now amended, more than one) component of the protein reaction system that is used to translate a desired protein is labeled (tagged or marked), and said desired protein is not labeled, that this particular cell free translation system can recover the translated protein from the rest of the proteins of the reaction system. Thus, the newly produced protein can be isolated because it has no tag, and the protein components of the reaction system can also be recovered because they are tagged, and said tags bind to an adsorbant which captures them. While this assertion that it is possible to recover the newly synthesized protein when all of the protein components of the reaction system are labeled may be true, the only flaw in the process is that when not all of the protein components of the reaction system are labeled then it will not be possible to directly isolate the nascent (newly synthesized) protein as it will be 'contaminated' with other protein components of the reaction system that also are not labeled. However, this may be a minor point.

1. Applicant's main argument regarding the Rothschild et al. reference is that they assert that it only discloses a method of incorporating a fluorescent protein markd into nascent proteins "via misaminoacylated tRNA's having the special fluorescent marker/$tRNA^{fmet}$". It is asserted that because this marker found in the nascent protein

that the protein can thus be isolated by said marker with avidin. And this contrary to the claimed invention where the protein produced is not labeled. However, the examiner does not feel this is a compelling argument. First, because the fact that protein that is produced is labeled or not labeled is of no consequence, the very minimum requirements of the claimed invention is that at least one or more of the reaction system proteins is labeled. There is no limitation in the claims stating that the protein produced is not labeled. Second, Applicant's have not read the reference as a whole. As stated in the previous Office action, Rothschild et al. teach a method of *in vitro* cell free protein synthesis of nascent polypeptides which are labeled. However, in order for the nascent polypeptide to obtain its label, a misaminoacylated tRNA with said label is added to the translation reaction system. (A "misaminoacylated tRNA" is defined on p. 8, paragraph 0087, and paragraph 0088, last two sentences. Misaminoacylation is the process whereby a tRNA molecule becomes charged. When this process occurs *in* vivo it is referred to aminoacylation, when it occurs by artifial means (e.g. specifically labeling the tRNA) it is referred to as misaminoacylation). The tRNA thus transfers said label to the nascent protein. The labeled tRNA is selected according to the choice of purification methods to be utilized for the protein, selected from the following: affinity chromatography, magnetic bead separation, chemical extraction, etc., *or* a combination of these techniques (see paragraph [0029] in Rothschild et al. (b) and column 7, lines 7-23 in Rothschild et al. (a)). Examples are given such as in paragraph [0165] of Rothschild et al. (b) where $tRNA^{fmet}$ is used to attach a fluorescent marker to the protein and (obviously the $tRNA^{fmet}$) which can subsequently be isolated by streptavidin affinity

purification methods. A variety of other affinity markers that are incorporated into the reaction system by introduction of the labeled misaminoacylated tRNA into the reaction system is outlined and described on p. 19 for Rothschild et al. (b) and under Affinity Markers and in column 35 line 25 for Rothschild et al. (a); such labels include lysine-tRNA that is labeled with biotin. The misacminoacylated tRNA's are incorporated into a cell free protein synthesis system by adding them to DNA and mRNA and all of the other components necessary to produce proteins. However, more than one marker can be incorporated and thus more than one type of misaminoacylated tRNA would have to be used (see p. 25 and paragraph 212 of 2005/0032078). In light of this disclosure, the examiner contends that Rothschild et al. does anticipate the instant claims because (a) as described above it is of no consequence if the protein produced in the reaction system is labeled, and (b) because Applicant's do not specify the protein components in the reaction system. Upon reading the claims in light of the specification, it is disclosed that members of the translation reaction system do not only include proteins, but also include enzymes and things such as $tRNA^{met}$. Thus it seems that Applicants also suggests labeling tRNA's. Furthermore, one skilled in the art would recognize that tRNA's are only capable of carrying a single amino acid at a time, thus when Rothschild et al. disclose using two different tRNA markers in order to insert two different markers into two different positions of the nascent protein, this necessarily means that two different tRNA's are used. For instance, the lysine-tRNA where the lysine is labeled with biotin is used along with $tRNA^{fmet}$ that is attached to a fluorescent marker, then this

necessarily means that more than one component of the reaction system is labeled. Thus, the limitations of the claims are satisfied.

35 USC § 102(b)

7. Applicant's arguments, see page 2-3, filed August 18, 2005, with respect to the anticipation of claims 1-17 by Allen et al. have been fully considered and are persuasive. Applicants have correctly pointed out that a *in vitro* transcription/translation system where the protein produced is tagged does not anticipate the claimed invention because the translated protein is not part of the reaction system. The rejection has been withdrawn.

Conclusion

8. Claims 1-17 are rejected. Claims 19-20 are objected to as being dependent upon a rejected base claim but would be allowable if rewritten in independent form.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suzanne M. Mayer, Ph.D. whose telephone number is 571-272-2924. The examiner can normally be reached on Monday to Friday, 7.30am to 4.00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SMM
28 October 2005

ROBERT A. WAX
PRIMARY EXAMINER